General

Guideline Title

Aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Mar. 65 p. (Technology appraisal guidance; no. 307).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Aflibercept in combination with irinotecan and fluorouracil-based therapy is not recommended within its marketing authorisation for treating metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen.

People currently receiving aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen should be able to continue treatment until they and their clinician consider it appropriate to stop.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Metastatic colorectal cancer

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Gastroenterology

Oncology

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To evaluate the clinical effectiveness and cost-effectiveness of aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy

Target Population

Patients with metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy

Interventions and Practices Considered

Aflibercept in combination with irinotecan and fluorouracil-based therapy

Major Outcomes Considered

- Clinical effectiveness
  - Overall survival (OS)
  - Progression-free survival (PFS)
  - Response rate
  - Adverse effects of treatment
  - Health-related quality of life (HRQoL)
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Centre for Reviews and Dissemination/Centre for Health Economics Technology Assessment Group, University of York (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of the Methods of Review(s)

Search Strategy

The manufacturer's submission (MS) described the search strategies used to identify relevant clinical effectiveness studies about the use of aflibercept for the treatment of metastatic colorectal cancer (mCRC) previously treated with an oxaliplatin-containing regimen.

The electronic databases MEDLINE and MEDLINE In-Process (via PubMed), EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to identify clinical studies on the use of aflibercept in the second-line treatment of mCRC. In addition to this, abstracts of conference proceedings from the American Society of Clinical Oncology (ASCO) and the European Society of Medical Oncology (ESMO) were reviewed.

Searches were conducted on 19 December 2012. The searches covered the period 1 January 1992 to December 2012, were limited to English language publications, and excluded animal studies. In addition, the EMBASE search strategy excluded all 'conference' publication types and the 'review' publication type. The manufacturer did not explain why the search was limited by date range and to only English language publications.

Overall the searches were appropriate and well documented, and included the use of both subject indexing terms (MeSH and EMTREE) and free text searching. Field searching, Boolean operators and truncation were used where required. All the databases required by NICE were searched, though only CENTRAL was searched in the Cochrane Library when it might have been useful to have searched the Cochrane Database of Systematic Reviews (CDSR), the Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment (HTA) database. Information about the EMBASE service provider was not provided, but was subsequently provided via the Points of Clarification letter.

There were some issues with the use of MeSH and EMTREE terms. The PubMed search strategy included both MeSH and Major MeSH index terms; Major MeSH terms are redundant when used alongside the equivalent MeSH terms. Further, the MeSH terms used ('Colorectal Neoplasms', 'Colonic Neoplasms' and 'Rectal Neoplasms') were not exploded, and so additional MeSH terms found further down the MeSH hierarchy would not have been searched for. In the EMBASE search strategy MESH terms are used instead of EMTREE terms in search line #1.

Other issues included: a missing Boolean operator (OR) in search line #2; a redundant search line (line #11); and unnecessary repetition of search terms (lines #4 and #36). The drug name aflibercept (and related terms) was not included in the search strategies and so it is possible that potentially useful records were not retrieved. The search strategies used in the manufacturer's submission were limited to RCTs and phase II and phase III trials, however a search for other study designs such as cohort or case control studies may have provided useful supplementary information about safety. It is not clear if the methodological search filters used in PubMed, EMBASE and the Cochrane Library were derived from validated search filters. The addition of the following EMTREE terms would have improved the filter used in EMBASE: 'Randomized Controlled Trial' and 'Controlled Clinical Trial'.

Despite the issues identified above, the searches were appropriate and comprehensive, and included the use of both subject indexing terms and free text searching. Field searching, Boolean operators and truncation were used where required. It is unlikely that any relevant studies have been missed. No separate search strategy was undertaken to identify relevant studies for the meta-analysis of the adverse effects of aflibercept.

Inclusion Criteria

RCTs of all current second-line chemotherapy regimens (including, but not limited to, bevacizumab; irinotecan; folinic acid/5-fluorouracil/irinotecan [FOLFIRI]; folinic acid/5-fluorouracil/oxaliplatin 4 [FOLFOX4]; FOLFOX6; capecitabine/oxaliplatin [capeOX, XELOX]) compared with placebo, best supportive care or the same or a different second-line chemotherapy regimen, for adult patients with mCRC were eligible for inclusion in the review. Trials had to assess outcomes relating to survival, progression, response, adverse effects or quality of life to be included in the review. Only English language articles were eligible for inclusion. The inclusion criteria were appropriate for a systematic review of all second-line chemotherapy regimens for adult patients with mCRC. It appears that at the study selection stage the inclusion criteria were narrowed down so that the only intervention eligible for inclusion in the review was aflibercept.

No inclusion criteria were presented for the meta-analysis of the adverse effects of aflibercept.

Cost-effectiveness

ERG Comment on Manufacturer's Review of Cost-effectiveness Evidence

Searches

The manufacturer's submission described the search strategies used to identify cost-effectiveness studies relevant to this appraisal of aflibercept for the treatment of mCRC. The review was performed as part of a wider systematic review aimed to identify utility, resource use and cost estimates relevant to the appraisal. Search strategies were only briefly described in the main submission, however full details were provided in the Appendix 10 of the MS.

The electronic databases MEDLINE and MEDLINE In-Process (via PubMed), EMBASE (Dialog), EconLit (EBSCO), the Cochrane Library (Wiley) including the NHS Economic Evaluation Database (NHS EED) and the Health Technology Assessment (HTA) database were searched. In addition to this, abstracts of conference proceedings from ASCO, ESMO, World Conference on Gastrointestinal Cancer, and International Society for Pharmacoeconomics and Outcomes Research (ISPOR) were searched. Regulatory organisation websites were also searched, including NICE, the Scottish Medicines Consortium (SMC), and the All Wales Medicines Strategy Group (AWMSG).

Database searches were performed on 27 June 2012. Internet searches were performed between 27 June and 6 July 2012. The searches covered the period 2010 to 27 June 2012. Searches were not performed for publications before 2010 because the NICE multiple-technology appraisal for cetuximab, bevacizumab, and panitumumab was published that year and provided relevant economic literature to that point. Further, the manufacturer did not expect there to be any aflibercept economic analyses prior to 2010. The searches were limited to English language publications, and excluded animal studies as well as the publication types 'review' and 'case reports', and the MeSH term 'Review Literature as Topic'.

The searches were appropriate and comprehensive, and included the use of both subject indexing terms and free text searching. Field searching, Boolean operators and truncation were used where required. All NICE required databases were searched, as well as abstracts of conference proceedings and regulatory body websites. An update of the searches closer to submission might have been useful.

Methodological search filters were included to identify economic studies and utilities in MEDLINE, EMBASE and the Cochrane Library. The economic study design search filter may have excluded potentially useful records from the NHS EED database in the Cochrane Library search as this database is already limited by study design.

Inclusion/Exclusion Criteria Used for Study Selection

The manufacturer undertook a series of systematic searches to identify published economic evaluations, including cost-effectiveness, and cost-utility analyses, as well as utility, resource use and cost studies. The ERG believes that the inclusion/exclusion criteria were appropriate, and would have identified any relevant studies.

Number of Source Documents

Clinical Effectiveness

One multicentre double-blind parallel-group randomised controlled trial (RCT) of aflibercept in combination with fluorouracil/leucovorin/irinotecan (FOLFIRI) compared with placebo and FOLFIRI was included in the review, the Aflibercept Versus Placebo in Combination With Irinotecan and 5-FU in the Colorectal Cancer After Failure of an Oxaliplatin Based Regimen (VELOUR) trial.

Cost-effectiveness

The manufacturer's systematic review did not identify any studies that evaluated the cost-effectiveness of aflibercept for patients with metastatic colorectal cancer (mCRC).

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Centre for Reviews and Dissemination/Centre for Health Economics Technology Assessment Group, University of York (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Data Extraction

Two reviewers independently extracted data from the included study, reducing the potential for error or bias. The manufacturer's submission (MS) presented adequate data from the Aflibercept Versus Placebo in Combination With Irinotecan and 5-FU in the Colorectal Cancer After Failure of an Oxaliplatin Based Regimen (VELOUR) trial.

Quality Assessment

The quality of the VELOUR trial was assessed using appropriate criteria specific to randomised controlled trials (RCTs), and a table of the quality assessment results was presented. Quality assessment results were checked by the ERG.

Evidence Synthesis

No meta-analysis of efficacy outcomes was undertaken as only one study of aflibercept in the second-line treatment of metastatic colorectal cancer (mCRC) was identified in the systematic review.

A meta-analysis of aflibercept adverse events was presented, including the VELOUR trial, the VITAL trial and the VANILLA trial.

Refer to Section 4 of the ERG report for additional information on clinical effectiveness (see the "Availability of Companion Documents" field).

Cost-Effectiveness

ERG Comment on Manufacturer's Review of Cost-effectiveness Evidence

Conclusions of the Systematic Review

There is a paucity of evidence on the cost-effectiveness of aflibercept. The only study, identified by the ERG, was conducted in the United States (US) and established a comparison against a treatment that was not considered a relevant comparator within this appraisal, and therefore of limited relevance. Furthermore, there is a lack of detail that precludes any formal quality assessment of the study.

Summary and Critique of Manufacturer's Submitted Economic Evaluation by the ERG

Model Structure

The *de novo* analysis presented by the manufacturer uses a three health state Markov model (see Figure 5 in the ERG report [see the "Availability of Companion Documents" field]). The three states are: i) Stable (non-progressive) disease; ii) Progressive disease (PD); and iii) Death. The stable state is further subpartitioned into "On second-line treatment" and "Discontinued second-line treatment". Patients enter the model in the stable state and the second-line treatment substate. At each 14 days cycle, patients can either remain on second-line treatment or can discontinue second-line treatment while continuing to remain stable. Patients can also transition through the model to progressive disease (PD) or Death from either of the stable states. No reversion from the PD state to the stable state is possible.

Refer to Table 5.1 of the ERG report (see the "Availability of Companion Documents" field) for a summary of the manufacturer's economic

evaluation. Refer to Section 5.2 of the ERG report (see the "Availability of Companion Documents" field) for more information on cost-effectiveness methods.

The Manufacturer's Economic Evaluation Compared to the NICE Reference Case Checklist

The manufacturer's base case economic evaluation meets the criteria of the NICE reference case checklist (see Table 5.2 of the ERG report [see the "Availability of Companion Documents" field]). No evidence synthesis was undertaken of efficacy outcomes as only one study of aflibercept in the second-line treatment of mCRC was identified in the systematic review. The ERG has been informed by their clinical advisor that other treatments (e.g., panitumumab, cetuximab and bevacizumab) are being used in clinical practice but it is not clear that this use could be considered representative of routine clinical practice, nor are any of these other treatments approved by NICE for this indication.

Refer to Section 5 of the ERG report for more information on cost-effectiveness analysis (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions on the Evidence for Cost-effectiveness

Availability and Nature of Evidence

The Committee concluded that overall the manufacturer's model adhered to the National Institute for Health and Care Excellence (NICE) reference case for assessing cost-effectiveness.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee considered that the manufacturer's assumption that the treatment benefit continues beyond the trial period and until 15 years is highly uncertain given that most patients had died during the 3-year follow-up period of the trial. The Committee considered that the Evidence Review Group's (ERG's) analysis that allows the hazard ratio to become greater than 1.0 could be considered implausible. The Committee agreed that the ERG's scenario, which assumes equal risk of death for all patients beyond the trial period (hazard ratio equals 1.0), represents an acceptable compromise between the 2 extremes of assuming continuing treatment effect (manufacturer's base case) and allowing for a reversed treatment effect (ERG's second scenario). The Committee noted that, in response to consultation, the manufacturer implemented a new scenario in its revised base case in which the hazard ratio begins to taper to 1.0 36 months after starting treatment, over a 12-month period. The Committee agreed that as a means to extrapolate overall survival both its preferred scenario (that is, the ERG's first scenario) and the manufacturer's new scenario were associated with some degree of uncertainty. In the absence of further evidence to validate the manufacturer's new approach, the Committee maintained its preference for the ERG's first scenario.

Incorporation of Health-Related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-Related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The Committee was aware that the manufacturer got the utility value for the stable-disease state from the 'mCRC utilities study' and revised it after consultation to a value derived from the ASQoP (an international single-arm open-label phase III study of aflibercept). The Committee noted that the ERG preferred another value from the ASQoP study for the stable-disease state. The Committee concluded that either value could be considered appropriate.

The Committee considered that the utility value chosen by the manufacturer for the progressed-disease state did not reflect the entire duration of progressed disease but only early progressed disease, and so was likely to be an overestimate. The Committee was aware that, in its base case, the ERG used an alternative lower value of 0.60, which had been used in the NICE guideline Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer (Technology appraisal guidance 118). The Committee agreed that no utility values for progressed disease were universally accepted as valid, but that it would be important that the utility value reflected the entire progressed-disease state. The Committee also agreed that adjusting the utility values for age was appropriate. The Committee concluded that the most plausible utility value for the progressed-disease health state would lie between the manufacturer's and the ERG's estimate.

The Committee concluded that all benefits of a substantial nature relating to treatment with aflibercept plus fluorouracil/leucovorin/irinotecan (FOLFIRI) had been captured in the quality-adjusted life year (QALY) calculation.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

Having considered the clinical evidence presented by the manufacturer for the 2 subgroups, the Committee concluded that it did not need to consider the cost-effectiveness of the technology for any of the subgroups.

What Are the Key Drivers of Cost-effectiveness?

The Committee considered the robustness of the mean overall survival benefit, obtained using the log-logistic function, of 3 months (5 years extrapolation time), 4.7 months (15 years extrapolation time) and 6.6 months (without truncating the survival curves).

The Committee was aware that the longer the time horizon, the greater the influence of the 'tails' of the extrapolation curves, which define the difference in mean overall survival between the treatment arms, and to which the model is highly sensitive.

The Committee noted that, because approximately three-quarters of the QALY gain in the model was accrued after disease progression, the model is highly sensitive to utility value for the progressed-disease state in the model.

Most Likely Cost-effectiveness Estimate (Given as an ICER)

The Committee noted that the manufacturer's incremental cost-effectiveness ratio (ICER) closest to its preferred assumptions was £44,000 per QALY gained (for age 60), but would increase for the higher age bracket, if the mean value was used from the manufacturer's survey of clinical oncologists after removing the outlier and if an extrapolation function with a less heavy tail had been used. Because the manufacturer's ICERs incorporated a utility value for progressed disease deemed by the Committee to be high, the Committee considered the ICER produced by the ERG using the Committee's preferred assumptions, but which used a utility value for progressed disease of 0.6. The Committee noted that this was approximately £51,000 per QALY gained and would be higher if an extrapolation function with a less heavy tail had been used. The Committee therefore concluded that the most plausible ICER was higher than the normally acceptable maximum ICER range of £20,000–30,000 per QALY gained.

Refer to Sections 3 and 4 in the original guideline document for additional information on cost-effectiveness.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of aflibercept and a review of this submission by the Evidence Review Group. For clinical effectiveness, one randomised controlled trial (RCT) was the main source of evidence. For cost-effectiveness, the manufacturer's model was considered.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy

Potential Harms

The summary of product characteristics lists the following most common adverse reactions (according to the Common Terminology Criteria for Adverse Events v3.0) for aflibercept plus fluorouracil/leucovorin/irinotecan (FOLFIRI) in order of decreasing frequency: leukopenia, diarrhoea, neutropenia, proteinuria, increased plasma activity of aspartate aminotransferase, stomatitis, fatigue, thrombocytopenia, increased plasma activity of

alanine aminotransferase, hypertension, weight loss, decreased appetite, epistaxis, abdominal pain, dysphonia, increased serum creatinine and headache.

For full details of adverse reactions, see the summary of product characteristics.

Contraindications

Contraindications

For full details of contraindications, see the summary of product characteristics.

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) has developed a costing statement explaining the resource impact of this guidance to help organisations put this guidance into practice. This tool is available from the NICE Web site (see also the "Availability of Companion Documents" field).

Implementation Tools

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Mar. 65 p. (Technology appraisal guidance; no. 307).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014 Mar

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Dr Amanda Adler (*Chair*), Consultant Physician, Addenbrooke's Hospital; Professor Ken Stein (*Vice Chair*), Professor of Public Health, University of Exeter Medical School; Dr Ray Armstrong, Consultant Rheumatologist, Southampton General Hospital; Dr Jeff Aronson, Reader in Clinical Pharmacology, University Department of Primary Health Care, University of Oxford; Professor John Cairns, Professor of Health Economics Public Health and Policy, London School of Hygiene and Tropical Medicine; Mark Chapman, Health Economics and Market Access Manager, Medtronic UK; Professor Fergus Gleeson, Consultant Radiologist, Churchill Hospital, Oxford; Robert Hinchliffe, HEFCE Clinical Senior Lecturer in Vascular Surgery and Honorary Consultant Vascular Surgeon, St George's Vascular Institute; Professor Daniel Hochhauser, Consultant in Medical Oncology, UCL Cancer Institute; Dr Neil Iosson, General Practitioner; Anne Joshua, Associate Director of Pharmacy, NHS Direct; Dr Rebecca Kearney, Clinical Lecturer, University of Warwick; Professor Ruairidh Milne, Director of Strategy and Development and Director for Public Health Research at the National Institute for Health Research (NIHR) Evaluation, Trials and Studies Coordinating Centre at the University of Southampton; Dr Elizabeth Murray, Reader in Primary Care, University College London; Dr Peter

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Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Aflibercept in combination with irinotecan and fluorouracil-based therapy for treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Mar. 1 p. (Technology appraisal guidance; no. 307). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Wade R, Duarte A, Simmonds M, Rodriguez-Lopez R, Duffy S, Spackman E, Woolacott N. Aflibercept in combination with irinotecan and fluorouracil-based therapy for the treatment of metastatic colorectal cancer which has progressed following prior oxaliplatin-based chemotherapy: a single technology appraisal. York (UK): CRD and CHE Technology Assessment Group; 2013. 140 p. Electronic copies: Available from the NICE Web site .

Patient Resources

The following is available:

- Aflibercept with chemotherapy for previously treated metastatic colorectal cancer. Information for the public: technology appraisals. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Mar. (Technology appraisal guidance; no. 307). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download as a Kindle or EPUB ebook from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on June 5, 2014.

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